NAPDH oxidase (NOXes) are membrane-bound enzymes that generate reactive oxygen species (ROS) that play a role in immune response and signaling. Misregulation of NOXes is implicated in various human pathologies. NOXes contain a catalytic core comprised of a heme-containing transmembrane (TM) domain and a cytoplasmic dehydrogenase (DH) domain that binds FAD and NADPH. Several conserved regions at the interface of the TM and DH domains in eukaryotic NOXes have been suggested to mediate enzyme function and activity. In 2017, researchers successfully purified SpNox, a bona fide NOX homolog from *Streptococcus pneumoniae and* verified its NOX properties. SpNox's robust activity in detergent makes it an excellent model system for studying NOXes. Using the SpNox model system, we investigate the role of the conserved, putative interacting regions at the TM:DH interface on enzyme activity. To probe the TM:DH interface, we purify and verify activity of the separate domains; create mutations in the conserved regions at the TM:DH interface; design peptides based on the putative interacting regions to inhibit TM:DH interactions. We conduct mixing experiments involving one wild-type domain and one mutant domain, in which we monitor heme reduction via an absorbance spectrum (350nm-700nm). Using peptides based on the conserved regions, we perform mixing experiments in which we mix the peptides with separate, wild-type TM and DH domains and assess its effects on TM:DH interactions. Understanding interdomain interactions using SpNOX may reveal potential druggable sites in the human NOXes and contribute to drug discovery.